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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,578	05/03/2002	Audrey Goddard	P3230R1C001-168	2392

30313 7590 10/31/2006

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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,578	GODDARD ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: Notice to Comply

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 8/24/06 has been entered.

Status of Application, Amendments and/or Claims

The 7/3/05 response and the 8/24/06 supplemental response have been entered. No claims are currently canceled, amended, or added. Claim 6 was previously canceled by Applicants.

Claims 1-5 are under consideration in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The Information Disclosure Statement of 7/3/06 has been fully considered.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, 37 CFR 1.821(c) states, "Patent applications which contain disclosures of nucleotide and/or amino acid sequences must contain, as a separate part of the disclosure, a paper copy disclosing the nucleotide and/or amino

acid sequences and associated information using the symbols and format in accordance with the requirements of § § 1.822 and 1.823." The instant application fails to comply with the requirements of 37 CFR 1.821(c) because the application file does not contain a paper copy of the Sequence Listing. It is noted that Applicants filed a computer readable form (CRF) of the Sequence Listing on 5/3/02; however, no paper copy of this listing has been submitted to date. In order to comply, Applicants are required to submit a paper copy of the Sequence Listing as well as a statement that the content of the paper and computer readable copies are the same and contain no new matter (see attached Notice to Comply).

Priority

The priority statement on the first page of the specification (starting at line 2; last updated by Applicants on 1/27/2006) contains two errors.

(1) The priority statement recites "...Application 10/006867 filed 12/6/2001, which is a continuation of, and claims priority under 35 USC § 120 to, PCT Application PCT/US00/23328 filed 8/24/2000..." However, a review of the continuity data for Application 10/006867 indicates that this application is actually a continuation-in-part (CIP) of PCT/US00/23328.

(2) The priority statement recites "...PCT/US00/23328 filed 8/24/2000, which is a continuation in part of, and claims priority under 35 USC § 120 to, US Application 09/380137 filed 8/25/1999, now abandoned..." However, a review of application 09/380137 indicates that this application was abandoned as an incomplete file and therefore was never granted a Filing or 371(c) Date. Therefore, the '137 application is not available for a priority claim in the instant application. In view of this, the instant application only merits priority to 8/24/2000, the filing date of PCT/US00/23328.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (4/19/2006).

The rejections of claims 1-5 under 35 U.S.C. § 101 at pg 2-10 for lacking utility, and under 35 U.S.C. § 112, first paragraph, at pg 10-11 for lacking enablement are

withdrawn in view of Applicants' persuasive arguments at pg 3-17 of the 7/3/06 response and pg 2-3 of the 8/24/06 supplemental response.

The claims of the instant invention are directed to an isolated antibody that specifically binds to the polypeptide of SEQ ID NO: 68. The specification provides several asserted utilities, including that the "PRO polypeptides of the present invention may be differentially expressed in a diseased tissue as compared to a normal tissue of the same tissue type" (pg 93, [¶ 0336]). Applicants argue that the gene expression data in the specification shows that the mRNA associated with the PRO1158 polypeptide was more highly expressed in normal lung tissue compared to lung tumor tissue (7/3/06 response; pg 2). In support, Example 18 demonstrates that PRO1158 cDNA (DNA6062-1507) is more highly expressed in normal lung as compared to lung tumor in this Example (pg 142). Identification of the differential expression of the PRO1158 polypeptide-encoding gene in tumor tissue compared to the corresponding normal tissue renders the molecule useful and enabled as a diagnostic tool for the determination of the presence or absence of tumor.

Applicants further assert "that it is well-established in the art that a change in the level of mRNA for a particular protein, *e.g.* a decrease, generally leads to a corresponding change in the level of the encoded protein, *e.g.* a decrease" (pg 4 of the 7/3/06 response). Applicants rely on more than 140 references (see IDS filed 01/27/06), where the mRNA expression levels of specific genes, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels.

It was previously argued in the 4/19/06 Office Action (pg 2-10) that mRNA levels were not predictive of protein levels (citing references by Chen et al, Futcher et al, Lian et al, Fessler et al) and that changes in mRNA levels did not produce corresponding changes in protein levels (citing comprehensive studies by Nagaraja et al, Waghray et al and Sagynaliev et al). However, each of these references measured mRNA levels by microarray analysis rather than quantitative PCR analysis, and the art recognizes that the results obtained by microarray are not always the same as the results obtained using quantitative PCR (for example, see Oda et al, 1997. Virchows Arch. 430: 99-105, specifically pg 104, column 1, ¶ 2). While the PTO found several references in which the

protein expression levels did not correlate with mRNA levels measured by quantitative PCR (see Sugg et al, 1998. Clinical Endocrinology 49: 629-637; Toler et al, 2003. Am J Obstet Gynecol. 194: e27-e31; Berner et al, 2003. Histopathol. 42: 546-554; Brooks et al, 2003. Am J Physiol Renal Physiol. 284: F218-F228), the majority of the references which were found, including those cited by Applicants, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels.

Applicants assert that the expression levels of protein correlate to mRNA (cDNA) levels when the cDNA is measured by quantitative PCR (i.e. rtPCR). Applicants have provided more than 140 references in support of this position. The prior art of record (Chen et al, Futcher et al, Lian et al, Fessler et al, Nagaraja et al, Waghray et al and Sagynaliev et al), argued by the Examiner, is not specifically directed to message levels measured by rtPCR. Based on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by rtPCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of nucleic acids encoding PRO1158, also supports a conclusion of differential expression of the PRO1158 polypeptide. Therefore, one of ordinary skill in the art would be able to use the PRO1158 polypeptide diagnostically for distinguishing lung tumor from normal lung tissue, as asserted by Applicants.

New Objections and/or Rejections

Specification

The disclosure is objected to because of the following informalities:

The priority statement contains two errors, as described above in the section titled "Priority".

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Baker et al, WO 00/63088, published December 9th, 1999 (12/9/1999). As noted above, in the section titled "Priority", the earliest date to which the instant application is entitled priority is August 24th, 2000 (8/24/2000).

It is noted that the '088 publication contains several inventors in common with the instant application. However, MPEP 2132.III states "The term "others" in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be "by others." This holds true for all types of references eligible as prior art under 35 U.S.C. 102(a) including publications as well as public knowledge and use."

The '088 publication teaches, in Figure 270, a PRO1158 protein sequence that is 100% identical to instant SEQ ID NO: 68. The '088 publication further teaches antibodies to the proteins of the invention, including antibodies that are monoclonal (pg 365); humanized (pg 367); fragments (pg 370); and labeled (pg 371). Therefore, the '088 publication clearly anticipates instant claims 1-5.

Claim Rejections - 35 USC § 103

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over NCBI Accession No. BE531149 (NCBI Accession No. BE531149, Strausberg, created August 7, 2000, updated August 9, 2000; cited in the 8/24/2000 Office Action) in view of U.S. Patent No. 6,262,234 (cited in the 8/24/2000 Office Action).

This rejection was previously set forth at pg 5-6 of the 8/24/2004 Office Action, and was withdrawn in the 1/13/05 Office Action in view of Applicants' argument that the

instant application merited priority to 6/22/98. However, as noted above in the section titled "Priority", the instant application only merits priority to 8/24/00. For this reason the previously withdrawn rejection is herewith reinstated.

Claims 1-5 are drawn to antibodies that bind to the polypeptide consisting of SEQ ID NO: 68. The antibodies can be monoclonal, humanized, fragments or labeled. NCBI BE531149 teaches a nucleic acid sequence that encodes a polypeptide that is 100% identical to SEQ ID NO: 68. The ATG representing the start codon of this protein is found at residues 15-17 of the nucleic acid sequence. The BE531149 accession number does not teach antibodies that bind to the encoded polypeptide.

The '234 patent teaches monoclonal antibodies, antigen-binding fragments, humanized antibodies, and labeled antibodies for use in characterizing novel polypeptides (see column 18). It would have been obvious to a person of ordinary skill in the art to make such antibodies because it is a commonly employed laboratory technique. One of ordinary skill in the art would have been motivated to do so because such antibodies are used for further characterization of novel polypeptides. The person of ordinary skill in the art would have had a reasonable expectation of success because the '234 patent teaches the techniques necessary to produce an antibody to a novel protein. Therefore, the invention taken as a whole is *prima facie* obvious over the prior art.

Note

In the 8/24/2004 Office Action at pg 5-6, claims 1-5 were rejected under 103(a) as being unpatentable over NCBI Accession No. AI889075 (NCBI Accession No. AI889075, Strausberg created July 26, 1999, updated September 1, 1999; cited in the 8/24/2000) in view of U.S. Patent No. 6,262,234 (cited in the 8/24/2000 Office Action). This rejection was withdrawn in the 1/13/05 Office Action in view of Applicants' argument that the instant application merited priority to 6/22/98. However, as noted above in the section titled "Priority", the instant application only merits priority to 8/24/2000. AI889075 has a publication date prior to this date. However, on further consideration it would not be obvious to use the nucleic acid sequence taught by

AI889075 to make antibodies that bind specifically to a protein of instant SEQ ID NO: 67. The nucleic acid sequence of AI8899075 contains a nucleic acid sequence that could theoretically be used to encode a protein with 92% homology to instant SEQ ID NO: 67. However, this potential "coding region" is a partial sequence, missing a start codon (ATG), and is out-of-frame and in reverse to the instant coding region. There is no specific teaching in the AI889075 that would lead one of skill in the art to reverse the sequence, add a start codon, and pick the out-frame sequence in order to encode a protein. Therefore, there is no motivation to make an antibody to a protein expressed from that particular region of the nucleotide.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Notice to Comply	Application No. 10/063578	Applicant(s) GODDARD ET AL	
	Examiner Zachary C. Howard	Art Unit 1646	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set by the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
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